

### ABSTRACT

Methods of detecting G protein-coupled receptor (GPCR) activity *in vitro* and *in vivo* are provided. In one embodiment, the method includes providing at least one cell that expresses a GPCR and a plurality of conjugated proteins. Each of the plurality of conjugated proteins is formed by conjugating an arrestin protein and a detectable molecule. The plurality of conjugated proteins are substantially evenly distributed in the cytoplasm of the at least one cell. A first image of the at least one cell is obtained by detecting an amount of energy emitted from the detectable molecules and storing a value relative to the amount of energy. The at least one cell is treated with an agonist. A second image of the at least one cell is obtained. The first image and the second image are compared to detect the localization of at least some of the plurality of conjugated proteins at endocytic vesicles and/or endosomes.